Patent
207/145

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| In re application of: | Group Art Unit: 1815 |
| ANDREW C. HIATT and FLOYD ROSE | Examiner: Griffin |
| Serial No.: 08/300,484 | |
| Filed: September 1, 1994 | |
| For: ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS USING PROTECTED NUCLEOTIDES | |



DECLARATION IN SUPPORT OF REQUEST FOR WITHDRAWAL OF NOTICE OF ABANDONMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I Jeffrey W. Guise declare as follows:

1. I am the attorney of record in the above-identified

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

| | |
|---|---|
| Kim Arnold-Cabello | |
| name of person mailing paper | |
| March 5, 1996 | K A Cabello |
| date of deposit | signature of person mailing paper |

SSSD/9366. v01

application, and have personal knowledge of the facts set forth herein and if called to testify, I would and could competently testify as follows:

2. A true and correct copy of the Response to the Office Action dated April 25, 1995 in the above-identified patent application is attached to this declaration as Exhibit A. This response was filed via first class mail on October 24, 1995. I prepared this Amendment and Response to the Examiner's Office Action and my signature appears on this response at page 8.

3. Exhibit B is a true and correct copy of the acknowledgment postcard mailed together with the response on October 24, 1995. The Patent & Trademark Office mail room stamp indicates the response was received in the Patent Office on October 27, 1995.

4. The documents attached as Exhibit A were mailed to the Patent Office on October 24, 1995, via first class mail as shown by the certificate of mailing found on both the Petition for Extension of Time and the Response.

5. I declare under the penalty of perjury under the laws of the United States that the foregoing is true and correct. I

make this declaration with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 100 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: March 5, 1996

Respectfully submitted,

LYON & LYON

By: _____
Jeffrey W. Guise
Reg. No. 34,613

First Interstate World Center
633 West Fifth Street
47th Floor
Los Angeles, CA 90071-2066
(213) 489-1600

EXHIBIT A

THE BANK OF CALIFORNIA, N.A.
660 So. Hope Street
Los Angeles, CA 90071

16-105
1220

# LYON & LYON

ATTORNEYS - AT - LAW

4250 EXECUTIVE SQUARE
SUITE 660
LA JOLLA, CA 92037

No. 2816

DOCKET NO. 207/145
SERIAL NO. 08/300,484
APPLICANT HIATT, ANDREW C.

| EXPLANATION | AMOUNT |
|---|---|
| EXT. OF TIME (3) | 450.00 |

PAY EXACTLY FOUR HUNDRED FIFTY DOLLARS AND NO/100-----

DATE OCTOBER 24, 1995 $ 450.00

TO THE ORDER OF COMMISSIONER OF PATENTS AND TRADEMARKS

LYON & LYON

Brenda G. Bernhardt

⑈002816⑈ ⑆122001055⑆ 032⑈058329⑈



**LYON & LYON**
LA JOLLA • CALIFORNIA

REMITTANCE ADVICE
PLEASE DETACH BEFORE DEPOSITING CHECK

TO COST OF EXT. OF TIME (3) 450.00 1-6516
RE: HIATT, ANDREW C./DOCKET NO. 207/145/SERIAL NO. 08/300,484
JGUI/KAC

THE BANK OF CALIFORNIA, N.A.
650 So. Hope Street
Los Angeles, CA 90071

16-105
1220

# LYON & LYON

ATTORNEYS - AT - LAW

4250 EXECUTIVE SQUARE
SUITE 660
LA JOLLA, CA 92037

No. 2815

DOCKET NO. 207/145
SERIAL NO. 08/300,484
APPLICANT HIATT, ANDREW C.

| EXPLANATION | AMOUNT |
|---|---|
| IDS | 220.00 |

PAY EXACTLY TWO HUNDRED TWENTY DOLLARS AND NO/100----

DATE OCTOBER 24, 1995 $ 220.00

TO THE ORDER OF COMMISSIONER OF PATENTS AND TRADEMARKS

LYON & LYON

Brenda C. Berthold

⑈002815⑈ ⑆122001055⑆ 032⑈058329⑈

WARNING: Original Document Has An Artificial Watermark On Reverse Side.

**LYON & LYON**
LA JOLLA • CALIFORNIA

**REMITTANCE ADVICE**
PLEASE DETACH BEFORE DEPOSITING CHECK

TO COST OF IDS 220.00 1-6516
RE: HIATT, ANDREW C./DOCKET NO. 207/145/SERIAL NO. 08/300,484
JGUI/KAC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| In re application of | Group Art Unit: 1815 |
| ANDREW C. HIATT and FLOYD R. ROSE | Examiner: Griffin |
| Serial No.: 08/300,484 | |
| Filed: September 1-, 1994 | |
| For: ENZYME CATALYZED TEMPLATE-INDEPENDENT CREATION OF PHOSPHODIESTER BONDS USING PROTECTED NUCLEOTIDES | |

## PETITION FOR EXTENSION OF TIME

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Applicants request an extension of time of 3 months to respond to the Office Action of April 25, 1995. Enclosed is the

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231

Kim Arnold-Cabello
(Type or print name of person signing paper)

Date of Mailing: October 24, 1995

K A Cabello
(Signature of person mailing paper)

EXHIBIT A

requisite fee of $450.00 as calculated below:

| | Small Entity | Other Than Small Entity |
|---|---|---|
| 1st month | ___ $ 55.00 | ___ $110.00 |
| 1st & 2nd month | ___ $190.00 | ___ $380.00 |
| 1st, 2nd & 3rd months | _X_ $450.00 | ___ $900.00 |

Please charge to Deposit Account No. 12-2475 any additional fees that may be required.

Date: October 24, 1995

Respectfully submitted,

LYON & LYON

By _____
JEFFREY W. GUISE
Registration No. 34,613

633 West Fifth Street
47th Floor
Los Angeles, CA 90071
(213) 489-1600



EXHIBIT A

Copy

207/145
Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | |
|---|---|
| In re Application of: | Group Art Unit 1815 |
| **Andrew C. Hiatt and Floyd R. Rose** | Examiner Griffin |
| Serial No. 08/300,484 | October 24, 1995 |
| Filed: September 1, 1994 | |
| For: Enzyme Catalyzed Template-Independent Creation of Phosphodiester Bonds Using Protected Nucleotides] | |

**RESPONSE**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In Response to the Office Action dated April 25, 1995, Applicant makes the following amendments and arguments. An extension of time has been concurrently filed with this Amendment and extends the time for taking action in response to the Office Action dated April

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231

Kim Arnold-Cabello
(Type or print name of person signing paper)

Date of Mailing: October 24, 1995

K A Cabello
(Signature of person mailing paper)

SSSD/742. v01

EXHIBIT A

25, 1995 to October 25, 1995. Also accompanying this Amendment is an Information Disclosure Statement which the applicant respectfully requests that the Examiner consider. The appropriate fee under §1.117(p) is also enclosed.

In The Claims

Please insert the word "and" in claim 14, line 5 before the word --- sulfones,--

Please amend claim 13 to depend from claim 12 by replacing the "1" in claim 13, line 1 with --12--.

Please amend claim 25 to depend from claim 24 by replacing the "19" in claim 25, line 1 with --24--.

Please amend claim 14 by inserting into line 3 after the word "phosphates" the word -- phosphoramide,--.

Please amend claim 21 to depend from claim 20 by replacing the "19" in claim 21, line 1 with --20--.

Please insert the symbol --®-- after the words "sepharose" and Fractosil" in claim 9, line 3.

A. Remarks

The Applicant respectfully requests that the Examiner enter the above-amendments into this Application. Applicants acknowledge the election of Group I, claims 1-31 with traverse made in a telephonic interview.



EXHIBIT A 1

The Examiner has stated that the method of claim 13 is encompassed by the method of claim 12 and that the method of claim 25 is encompassed by the method of claim 24. The claims have been amended to make claim 13 dependent on claim 12 and to make claim 25 dependent on claim 24.

The Examiner has pointed out that claim 15 lacks an antecedent basis. In claim 24 with respect to the term "a phosphorous containing moiety". Claim 14 has been amended to include the term "phosphoramide".

The Examiner has pointed out that claim 21 lacks an antecedent basis in claim 19 upon which it is dependent for "cations". Claim 21 has been amended to depend on claim 20 and therefore provide the proper antecedent basis for the term "cations".

In addition, the Examiner has objected to the use of the Sepharose and Fractosil in claim 9 without the accompanying trademark symbols. Claim 9 has been amended to correct this informality.

1. Rejection of Claims 1-31 Under 35 U.S.C. §112, Second Paragraph

Claims 1-31 of the instant application have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner states that the claims are indefinite and unduly broad because of the expressions "a



EXHIBIT A

polynucleotide of a predetermined sequence" and the term "an initiating substrate". Applicants respectfully traverse this rejection.

The term "polynucleotide of a predetermined sequence" is described at page 30, lines 14-21 of the specification. One of ordinary skill in the art upon reaching that description would understand this term to mean that the order in which the individual nucleotides were added to the initiating substrate using the reactions of the present invention were selected so that when the synthesis is completed, a polynucleotide having a preselected sequence was produced. One of ordinary skill in the art is readily familiar with the concept of a predetermined nucleotide sequence. The predetermined sequence may be any nucleotide sequence as long as it is selected prior to the initiation of the synthesis reaction. In addition, one of ordinary skill in the art understands that a predetermined nucleotide sequence could include a sequence in which a randomly selected nucleotide has been inserted into the sequence at one or more positions within that sequence. One of ordinary skill in the art would recognize that a predetermined nucleotide sequence containing random nucleotides at one or more positions are useful in certain molecular biology procedures. It is therefore respectfully submitted that the term "polynucleotide of a pre-determined sequence" as used in the claims and understood by one of ordinary skill in the art is not indefinite. Applicant respectfully requests that the Examiner withdraw this rejection.

The term "an initiating substrate" is described at pages 14, line 6 - page 17, line 1 of the specification. Specifically, at page 14, lines 9-34, of the specification describes the



EXHIBIT A

requirements for the initiating substrate of the present invention. One of ordinary skill in the art, upon reading this description, would understand the requirements for an initiating substrate in the context of the present invention and claims. In general, initiating substrates contain a nucleoside with a free and unmodified 3'-hydroxyl group. It is at this 3' hydroxyl group that the subsequent addition of nucleotides occurs. The specification describes various embodiments and permutations of useful initiating substrates including, the termini of polynucleotides which are generated using standard molecular biology techniques including the termini of DNA or RNA vectors, single-stranded or double-stranded DNA fragments, single-stranded or double-stranded RNA fragments and RNA or DNA oligonucleotides. The present invention contemplates a variety of initiating substrates each having the required nucleoside with a free and unmodified 3'-hydroxyl group. One of ordinary skill in the art would understand the description of these various initiating substrates provided in the specification. It is therefore respectfully submitted that the Examiner withdraw this rejection.

2. Rejection of Claims 30 and 31 Under 35 U.S.C. § 102(b)

Claims 30 and 31 have been rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Miyoshi et al., (U.S. Patent 4,605,735), Frank et al., (U.S. Patent 4,689,405), and Andrus et al. (U.S. Patents 4,816,571 and 5,047,524). The Examiner states that there is no patentable distinction between the polynucleotides produced by the processes disclosed in Miyoshi, Frank , or Andrus. The applicant respectfully traverses this rejection.



EXHIBIT A

U.S. Patent 4,605,735 to Miyoshi et al. describes a method of preparing polynucleotides which have either biotin or 2,4-dinitrophenyl attached to its 5' end. The polynucleotides produced by Miyoshi et al. are clearly distinguishable from the polynucleotides produced by the present invention. The polynucleotides produced by the present invention do not contain biotin or 2,4-dinitrophenyl attached to the 5' position of the 5'-most nucleotide. Thus, the polynucleotides of the present invention are distinguishable from those of Miyoshi et al.

U.S. Patent 4,689,405 to Frank et al. discloses methods for synthesizing oligonucleotides attached to solid phase supports. Frank et al. disclose attaching nucleotides via the 3' position of a nucleotide to the solid phase support. The polynucleotides of the present invention are clearly distinguishable from the Frank et al. polynucleotides because the process of the present invention produces a polynucleotide attached via its 5' position to the solid support. The remainder of the polynucleotide is then attached to that first nucleotide. Thus, the polynucleotides produced by the methods of the present invention are clearly distinguishable from those of Frank et al.

U.S. Patents 4,816,571 and 5,047,524 to Andrus et al. describe methods for producing polynucleotides on a solid support. The Andrus et al. methods link the 3' position of a nucleotide to a solid support and synthesizing the polynucleotide using the nucleotide which is attached to the solid support as the starting nucleotide. The methods of Andrus et al. produce polynucleotides which are attached via the 3' position of a nucleotide to a solid support. The



EXHIBIT A

Andrus et al. polynucleotides are thus clearly distinguishable from the polynucleotides produced by the methods of the present invention. When the present invention utilizes a solid support, the oligonucleotide is attached to the solid support via the 5' position of that nucleotide. The polynucleotide is then synthesized using this 5'-attached nucleotide as a starting point. Therefore, the Andrus et al. polynucleotides are clearly distinguishable from those of the present invention.

Based on the above remarks, Miyoshi et al., Frank et al., and both Andrus et al. patents do not anticipate the polynucleotides of the present invention. The processes described in these references and the polynucleotides produced by those processes are distinguishable from those of the present invention in that they produce the polynucleotides in the reverse direction (3' to 5'), produce polynucleotides which have a biotin or 2,4-dinitrophenol moiety attached to the 5' nucleotide, or produce polynucleotides which are attached to a solid support via the 3' position of the 3'-most nucleotide. The present invention does not produce polynucleotides in this manner and the polynucleotides produced do not contain these particular moieties attached to the 5'-most nucleotide or to the 3'-most nucleotide.



EXHIBIT A

Based on the above amendments and remarks, the applicant believes that the present claims are in condition for allowance. Applicant respectfully requests early notification thereof.

Respectfully submitted,

LYON & LYON

By _____
Jeffrey W. Guise
Reg. No. 34,613

First Interstate World Center
633 West Fifth Street, 47th Floor
Los Angeles, CA 90071-2066
(213) 489-1600



EXHIBIT A